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**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Paper No. 21

Application Number: 08/869,386

Filing Date: June 5, 1997

Appellant(s): Sastry et al.

Stephen Hash
For Appellant

EXAMINER'S ANSWER

This is in response to appellant's brief on appeal filed Mar. 31, 2000.

(1) *Real Party in Interest*

A statement identifying the real party in interest is contained in the brief.

(2) *Related Appeals and Interferences*

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

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(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellant's statement of the issues in the brief is substantially correct.

The issues are:

a. Claims 29-45 and 47 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inhibiting HIV entry into a cell *in vitro* comprising contacting the cell with peptides consisting of SEQ ID NOs: 1, 3, or 5, does not reasonably provide enablement for a method of inhibiting HIV entry into a cell *in vivo* employing all of the possible claimed peptide sequences is maintained for reasons of record.

b. Claim 49 is rejected under 35 U.S.C. 102(e) as being anticipated by Berzofsky et al. (U.S. Pat. No. 5,820,865).

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(7) *Grouping of Claims*

Claims 29-45 and 47 stand or fall together with regards to the 112 rejection. Claim 49 stands alone with regard to the 102 rejection.

(8) *ClaimsAppealed*

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) *Prior Art of Record*

The following is a listing of the prior art of record relied upon in the rejection of claims under appeal.

5,820,865

Berzofsky et al.

Oct. 13, 1998

(10) *Grounds of Rejection*

The following ground(s) of rejection are applicable to the appealed claims:

a. Claims 29-45 and 47 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inhibiting HIV entry into a cell *in vitro* comprising contacting the cell with peptides consisting of SEQ ID NOs: 1, 3, or 5, does not reasonably provide enablement for a method of inhibiting HIV entry into a cell *in vivo* employing all of the possible claimed peptide sequences is maintained for reasons of record.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The claims are drawn to a method of directly inhibiting HIV entry into a cell comprising contacting the cell with a composition comprising a peptide of 8-24

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residues comprising SEQ ID NO:5. The specification at pages 65-67 and Fig. No. 8 disclose culturing MT-4 cells and primary human T cells in the presence of HIV and a selected peptide from the V3 loop of gp120 and the reverse transcriptase assays showed a decrease in the amount of reverse transcriptase produced in the cells incubated with certain peptides. However, the specification does not show a correlation between that which occurred *in vitro* to that which one of skill in the art would reasonably expect *in vivo*.

The specification provides no probative evidence to support the claimed treatment which would protect humans against HIV infection. The obstacles to treatment development and therapeutic approaches with regard to retroviruses associated with AIDS in humans are well documented in the literature. These obstacles include: 1) the extensive genomic diversity associated with the HIV retrovirus, particularly with respect to the gene encoding the envelope protein, 2) the fact that the modes of viral transmission include virus-infected mononuclear cells, which pass the infecting virus to other cells in a covert form, as well as via free virus transmission, 3) existence of a latent form of the virus, 4) the ability of the retrovirus to "hide" in the central nervous system where blood cells and neutralizing agents carried by the blood cannot reach the retrovirus, due to the blood-brain barrier and 5) the complexity and variation of the elaboration of the disease. The existence of these obstacles establish that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any vaccine or any immunization treatment or any therapeutic regimen on its face. In order to enable claims to drugs and their uses, either *in vivo* or *in vitro* data, or a

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combination of these can be used. However, the data must be such as to convince one of ordinary skill in the art that the claims are sufficiently enabled. When the claims are directed to humans adequate animal data would be acceptable in those instances wherein one of ordinary skill in the art would accept the correlation to humans. Thus in order to rely on animal data there must exist an art-recognized animal model for testing purposes. See *In re Hartop*, 311 F.2d 249, 135 USPQ 419 (CCPA 1962).

Yarchoan et al. (J. Enz. Inh., 1992) state that while a number of agents have been found to block HIV binding to the target cell in vitro, these agents have generally not shown clear-cut evidence of clinical activity (abstract). Moreover, Gait et al. (TIBTECH 1995) discuss the problems associated with protein therapies for HIV and state that they suffer from problems of short serum half-life, poor bioavailability, and rapid clearance. Gait et al. also teach that as these problems were overcome, other problems emerged such as sequestration of the drug by serum proteins, drug resistance, and uneven distribution throughout the body, and that since these types of problems are unpredictable, it remains necessary to take into account the pharmacological parameters (p. 437).

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in *In re Wands*, 8 USPQ 2d 1400 at 1404 (CAFC 1988).

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(2) (3)

In the instant specification, it is determined that: 1) there are no working examples which suggest the desired results of inhibiting HIV infection *in vivo*, 2) the nature of the invention involved the complex and incompletely understood area of immunity to HIV, 3) the state of the prior art shows that prior treatment methods have been largely ineffective for the intended purpose, 4) the relative skill of those in the art is commonly recognized as quite high (post-doctoral level), and 5) the lack of predictability in the field to which the invention pertains is recognized in the art as evidenced by prior failures. In view of all of the above, it is determined that the specification is not commensurate in scope with the claimed invention.

b. Claim 49 is rejected under 35 U.S.C. 102(e) as being anticipated by Berzofsky et al. (U.S. Pat. No. 5,820,865). The claim is drawn to a method for directly inhibiting HIV entry into a cell *in vitro* comprising contacting the cell with a peptide comprising a specific sequence. It should be noted that the phrase "for directly inhibiting HIV entry into a cell" is viewed as an intended use and is given little patentable weight. Berzofsky et al. disclose a method for protecting cells from HIV comprising contacting cells *in vitro* with a composition that comprises a peptide having the claimed sequence (cols. 3-4). The method of Berzofsky et al. is the same as the claimed method. Therefore, Berzofsky et al. anticipate the invention as claimed.

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(II) Response to Argument

a. Regarding the rejection of claims 29-45 and 47 under 35 U.S.C. 112, first paragraph, appellant urges that *in vitro* and *in vivo* data have been presented which enable the claimed invention, the *in vivo* data presented in the Arlinghaus declaration employs an accepted animal model, and Fultz, 1993 teaches that the chimpanzee is an acceptable model for HIV in humans.

This is not found persuasive because, as previously stated, Haynes (Science 1993) states that "in spite of an extraordinary amount of work in search of an animal model for human AIDS , no animal model exactly mirrors HIV infection". Haynes also states that the immune correlates of animal models to human regarding AIDS are not known (p. 1280 1st. col. 1st and 2nd. para.s) . Haynes, et al. (Ann. Med., 1996 p. 40) teach that major scientific obstacles blocking the development of successful HIV treatments are the extraordinary variability of HIV, the lack of an exact animal model of HIV-induced AIDS, and the lack of understanding of the correlates of protective immunity to HIV (p 1280). Regarding the use of *in vitro* data, Ex parte Balzarini, 21 USPQ 2d 1892 (BPAI, 1991) states that persons skilled in the art would question claims for *in vivo* treatment of retroviral diseases, AIDS, or AIDS-related diseases based upon *in vitro* testing, since references show that those skilled in art would not associate successful *in vitro* results with successful *in vivo* treatment of AIDS. It is clear that one of skill in the art at the time of applicant's invention would not have expected *in vitro* data or *in vivo* data employing chimpanzees to correlate to humans. While Fultz et al. discusses

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using chimpanzees as a model for screening potential HIV treatments and that chimpanzees can become infected with HIV, Haynes et al., 1996 (which was published three years after Fultz et al.) states that current animal models of either HIV or simian (such as the chimpanzee) fall short of precisely mirroring HIV infection in humans (p. 41, 2nd complete par.).

Additionally, Gait et al. (TIBTECH 1995, published two years after Fultz et al.) discuss the problems associated treating HIV infection in humans with peptide therapies and state that peptide therapies suffer from problems of short serum half-life, poor bioavailability, and rapid clearance. Gait et al. also teach that as these problems were overcome, other problems emerged such as sequestration of the drug by serum proteins, drug resistance, and uneven distribution throughout the body, and that since these types of problems are unpredictable, it remains necessary to take into account the pharmacological parameters (p. 437). Therefore, it

is clear that one of skill in the art at the time the invention was made would not have expected *in vitro* or *in vivo* data to correlate to directly inhibiting HIV infection in human cells.

Moreover, the claims recite a method of protecting human cell from HIV infection which reads on a vaccine for HIV. Regarding the state of HIV vaccine as of 1993, well after filing date of the present invention, Wright states that because of the high degree of genetic, antigenic variations in such viruses, no one has yet, years after the invention, developed a generally successful AIDS virus vaccine. Wright 999 F. 2d at 1561, 27 USPQ2d at 1513.

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Appellant further urges peptides are an accepted means of inhibiting viral uptake and cites Vitetta et al. and Sabatier et al. and a closely related peptide is now in phase II clinical trials.

This is not found persuasive because Yarchoan et al. (J. Enz. Inh., 1992) state that while a number of agents have been found to block HIV binding to the target cell in vitro, these agents have generally not shown clear-cut evidence of clinical activity (abstract). Moreover, Gait et al. (TIBTECH 1995) discuss the problems associated with peptide therapies for HIV and state that they suffer from problems of short serum half-life, poor bioavailability, and rapid clearance. Gait et al. also teach that as these problems were overcome, other problems emerged such as sequestration of the drug by serum proteins, drug resistance, and uneven distribution throughout the body, and that since these types of problems are unpredictable, it remains necessary to take into account the pharmacological parameters (p. 437). Additionally, it is well known, as shown by the attached FDA 257a study that Phase II studies are concerned with safety and not treatment of disease. It should be noted that the two patents cited by appellant do not claim a method of directly inhibiting HIV infection into a human cell and are not within the scope of the claimed invention.

Appellant further urges that the Arlinghaus declaration shows inhibition of HIV replication which denotes an inhibition of cellular infection rather than prevention of host infection.

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This is not found persuasive because the Arlinghaus declaration states that the peptides inhibit HIV replication *in vitro* or in chimpanzees which is not the same as directly inhibiting HIV infection. Therefore, the declaration is not commensurate in scope with the claimed invention.

Furthermore, Appellant urges the working examples in the specification and the teachings of the specification enable the invention as claimed.

This is not found persuasive because, as stated above, Haynes (Science 1993) states that "in spite of an extraordinary amount of work in search of an animal model for human AIDS , no animal model exactly mirrors HIV infection". Haynes also states that the immune correlates of animal models to human regarding AIDS are not known (p. 1280 1st. col. 1st and 2nd. para.s) . Haynes, et al. (Ann. Med., 1996 p. 40) teach that major scientific obstacles blocking the development of successful HIV treatments are the extraordinary variability of HIV, the lack of an exact animal model of HIV-induced AIDS, and the lack of understanding of the correlates of protective immunity to HIV (p 1280). Regarding the use of *in vitro* data, Ex parte Balzarini, 21 USPQ 2d 1892 (BPAI, 1991) states that persons skilled in the art would question claims for *in vivo* treatment of retroviral diseases, AIDS, or AIDS-related diseases based upon *in vitro* testing, since references show that those skilled in art would not associate successful *in vitro* results with successful *in vivo* treatment of AIDS. It is clear that one of skill in the art at the time of applicant's invention would not have expected *in vitro* data or *in vivo* data employing chimpanzees to correlate to humans.

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b. Regarding the rejection of claim 49 is rejected under 35 U.S.C. 102(e) as being anticipated by Berzofsky et al., appellant urges that the mechanisms of protection sought by the claimed invention and the Berzofsky et al. patent are different, Berzofsky et al. fail to teach expressly or inherently each limitation of the claimed invention and one of ordinary skill in the art would not extrapolate from the reference that the method be used for directly inhibiting viral entry.

This is not found persuasive because the claim is drawn to a method for directly inhibiting HIV entry into a cell *in vitro* comprising contacting the cell with a peptide comprising a specific sequence. The phrase "for directly inhibiting HIV entry into a cell" is viewed as an intended use and is given little patentable weight. In response to applicant's arguments, the recitation "for directly inhibiting HIV entry into a cell" has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone.

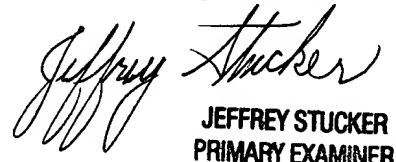
In re Hirao, 535 F.2d 67, 190 USPQ 15 (CCPA 1976); Kropa v. Robie , 88 USPQ 478, 481

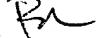
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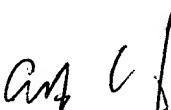
(CCPA 1951). As previously stated, Berzofsky et al. disclose a method for protecting cells from HIV comprising contacting cells *in vitro* with a composition that comprises a peptide having the claimed sequence (cols. 3-4). The claims are broadly written and do not recite the mechanism for inhibiting infection of the cell. Therefore, since the method of Berzofsky et al. employs the same active ingredient and the same step, it is the same as the claimed method. In conclusion, Berzofsky et al. anticipate the invention as claimed.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,


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April 21, 2000


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